Remarks

The present invention is directed to methods of inhibiting cytokine or biological activity of MIF. Claims 3-17, 24, 25 and 31-40 have been cancelled. CLaims 41-43 are newly added. Claims 1-2, 18-23, 26-30 and 41-43 are currently pending.

Rejections under 35 U.S.C. 112, 1st paragraph

Claims 1, 19, 26 and 28-30 are rejected under 35 U.S.C. 112, first paragraph, because the Examiner asserts that the specification, while being enabling for making salts of the claimed compounds, does not reasonably provide enablement for making prodrugs of the claimed compounds.

The claims have been amended to remove the term prodrugs. Accordingly, this rejection is moot.

Claims 1-23 and 26-30 are rejected under 35 U.S.C. 112, first paragraph, because the Examiner asserts that the specification does not enable one skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. Applicants respectfully traverse this rejection as it applies to the amended claims.

The Examiner rejected claims 1-23 and 26-30 for lacking enablement specifically due to the unpredictability of treating rheumatoid arthritis in patients, and in addition the many different types of diseases claims in the application which all have different mechanisms of action and accordingly could not be said to share the same method of treatment.

The compounds of the invention have been shown to be MIF antagonists. As noted by the Examiner, the specification provides assay data showing the ability of the compounds of the

invention to inhibit the action of MIF. A number of conditions are known to involve MIF activity and accordingly the use of the MIF antagonists of the present invention to antagonize MIF in conditions in which MIF has been shown to have a role, is enabled. For example, Leech, M., et al., Arthritis and Rheumatism (1999) 42:1601-1608 and Morand, E.F., et al., Rheumatology (Oxford, England) (2002) 41(5):558-562 show the role of MIF activity in rheumatoid arthritis. Applicants enclose the following list of literature publications which support the role of MIF in a variety of diseases which have been recited in claims 21 and 22. These references are provided in the Information Disclosure Statement that accompanies this Response.

1.	Rheumatoid arthritis	Morand et al., (2003)
2.	Systemic lupus erythematosus	Sanchez et al., (2006)
3.	Atherosclerosis	Pan et al. (2004)
4.	Myocardial infarction	Yu et al., (2003)
5.	Hepatitis	Kobayashi et al., (1999)
6.	Endotoxic and septic shock	Calandra et al., (2000)
7.	Asthma	Magalhaes et al., (2007)
8.	Colorectal carcinoma	He et al., (2009)
9.	Diabetes mellitus	Stosic-Grujicic et al., (2008)
10.	Inflammatory bowel disease including ulcerative colitis and Crohn's disease	de Jong et al., (2001)
11.	Multiple sclerosis	Denkinger et al., (2003)
12.	Glomerulonephritis	Lan et al., (1997)
13.	Prostate cancer	Meyer-Siegler et al., (2005)
14.	Lung carcinoma	Rendon et al., (2007)
15.	Non-melanoma skin cancer	Martin et al., (2008)
16.	Malignant melanoma	Shimizu et al., (1999)
17.	Lymphoma	Chesney et al., (1999)
18.	Osteoporosis	Onodera et al., (2006)
19.	Wound healing	Hardman et al., (2005)
20.	Psoriasis	Shimizu et al., (2001)
21.	Childhood nephritic syndrome	Berdeli et al., (2005)
22.	Breast carcinoma	Xu et al., 2008)
23.	Juvenile arthritis	De Benedetti et al., (2003)
24.	Systemic sclerosis	Selvi et al., (2003)
25.	Ovarian cancer	Hagemann et al., (2007)
26	Ceoliac disease	Nunez et al., (2007)

27.	Uveitis	Kotake et al., (2002)
28.	Diabetic retinopathy	Tashimo et al., (2004)
29.	Hepatocellular carcinoma	Ren et al., (2003)
30.	Gastric carcinoma	Shun et al., (2005)
31.	Oesophageal squamous cell carcinoma	Ren et al., (2005)
32.	Bladder cancer	Meyer-Siegler et al., (2004)
33.	Nasopharyngeal carcinoma	Suzuki et al., (2005)

In view of the list above, and Applicants description of the compounds used in the claimed method, one of ordinary skill in the art would be able to make and use the claimed invention commensurate with the scope of the claims with a reasonable expectation of success. The legal standard for enablement is met. Withdrawal of this rejection is respectfully requested.

Claims 1-17, 19-23 and 26-30 are rejected under 35 U.S.C. 112, first paragraph, because the Examiner asserts that the specification although enabling for a compound of formula (I), wherein the compound is a specific benzimidazole derivative, wherein a specific alkyl chain is present off the benzimidazole ring, it is not enabled for other definitions. Applicants respectfully traverse this rejection as it applies to the amended claims. The claims have been amended to more specifically claim the compositions used in the claimed methods. Reconsideration by the Examiner, and withdrawal of this rejection is respectfully requested.

Obviousness-type Double Patenting

Claims 1-23 and 26-30 are rejected for obviousness-type double patenting over claims 1-27 of U.S. Patent Application 12/158,563. Applicants respectfully request deferral of this rejection until allowable subject matter is found in either patent application. At such a time, a terminal disclaimer will be filed if deemed necessary.

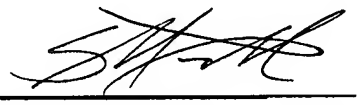
Conclusions

Applicants submit that the response herein provides a complete response to the Restriction Requirement dated November 20, 2008.

If the Examiner believes there are other issues that may be resolved by telephone interview, or that there are any informalities remaining in the application that may be corrected by Examiner's Amendment, a telephone call to the undersigned is respectfully solicited.

No additional fees are believed due, however the Commissioner is hereby authorized to charge any additional fees that may be required, or credit any overpayment of fees to Deposit Account number 11-0980.

Respectfully submitted,



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Date: March 20, 2009

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